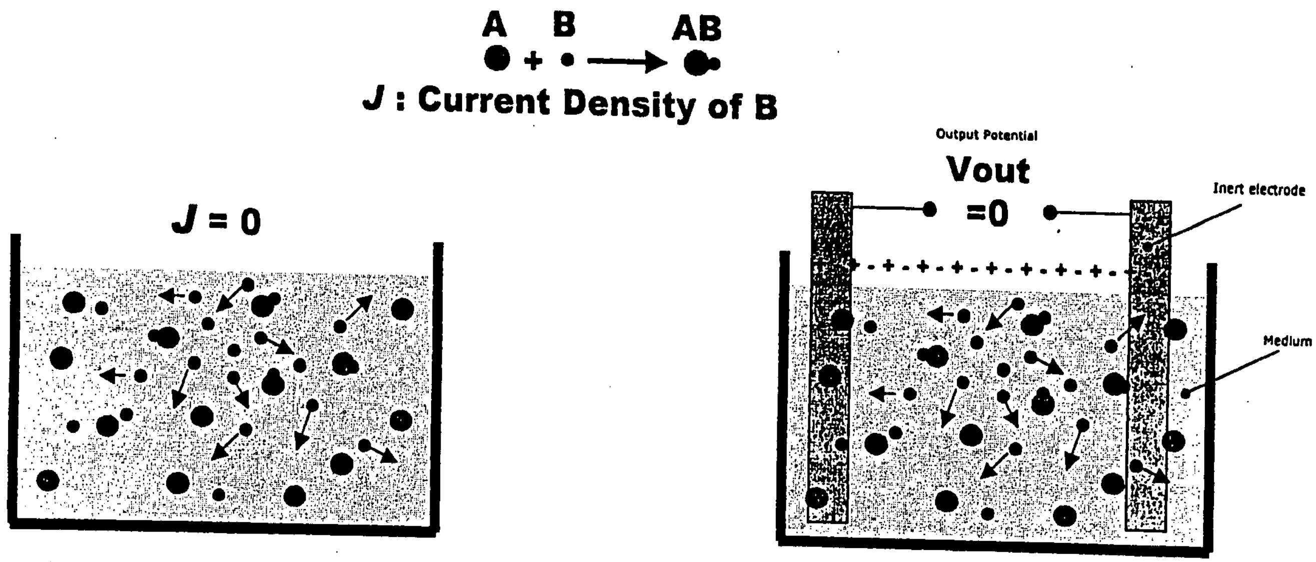
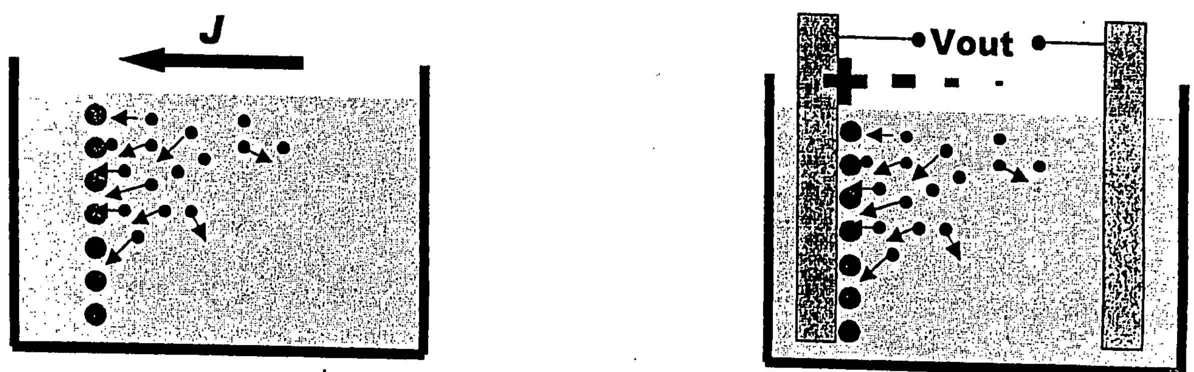
1.1



1.1) If A and B are both free in the medium no net transient gradient of molecules (current density) is created.

1.2



1.2) If A is spatially immobilized and B is free in the medium, the reaction causes a net transient gradient (current density) of B toward A. This transient current creates a temporary potential difference in the medium.

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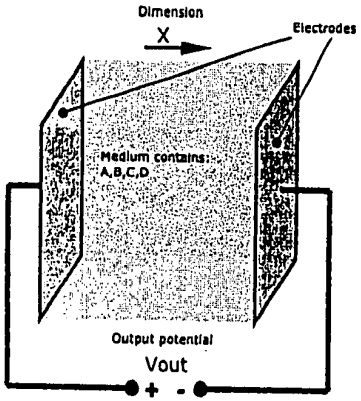
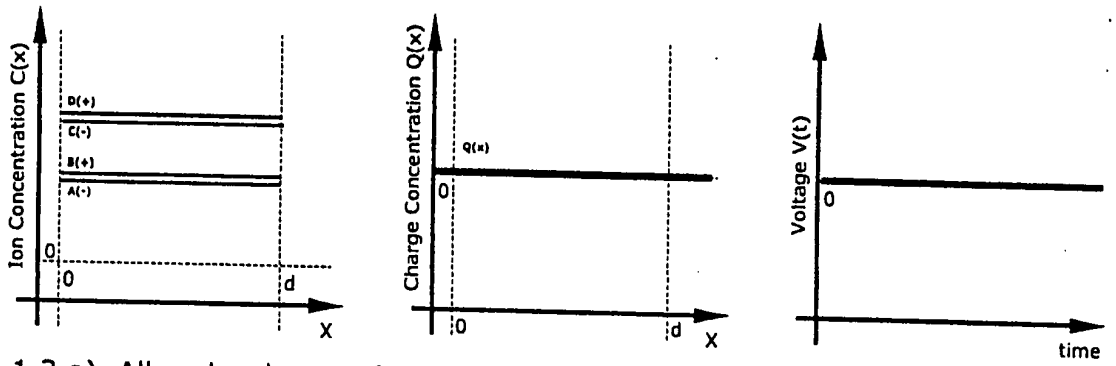
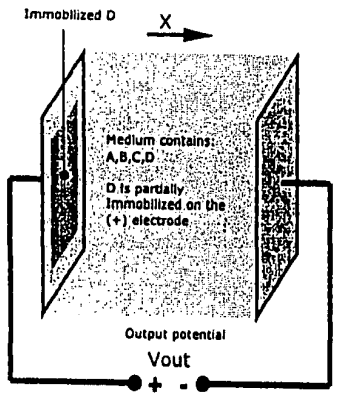
1.3 Potential difference between electrodes equilibrium (steady state):

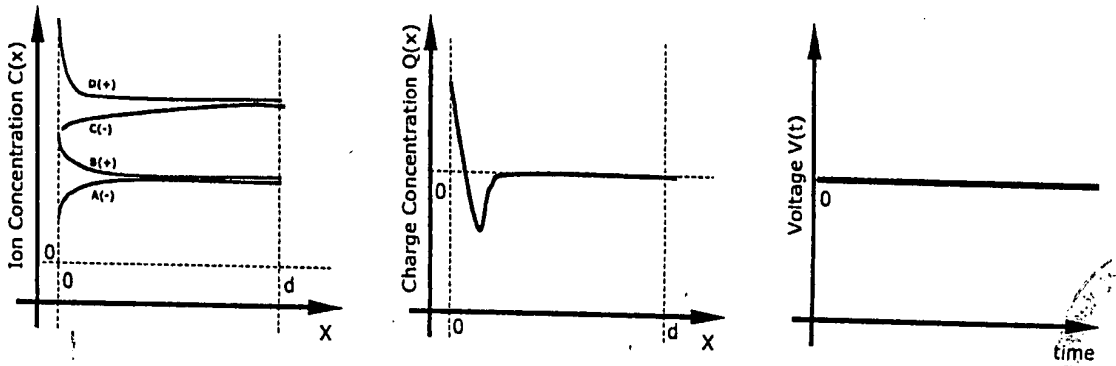
1) Electrodes are inert and do not interact with medium.
2) Four molecules (ions) A, B, C and D are present in the medium.
3) Molecules have arbitrary diffusion length and charge.





1.3.a) All molecules are free in the medium. Concentration of all molecules is uniform in equilibrium.





1.3.b) D is partially immobilized on the surface of the (+) Electrode which forces a none uniform concentration of molecules.

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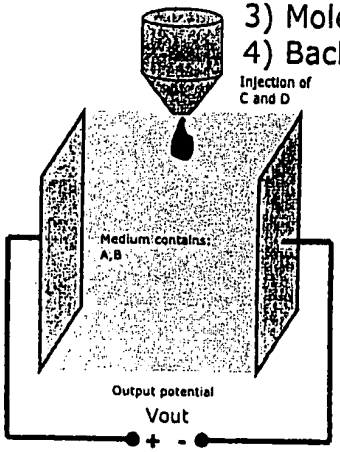
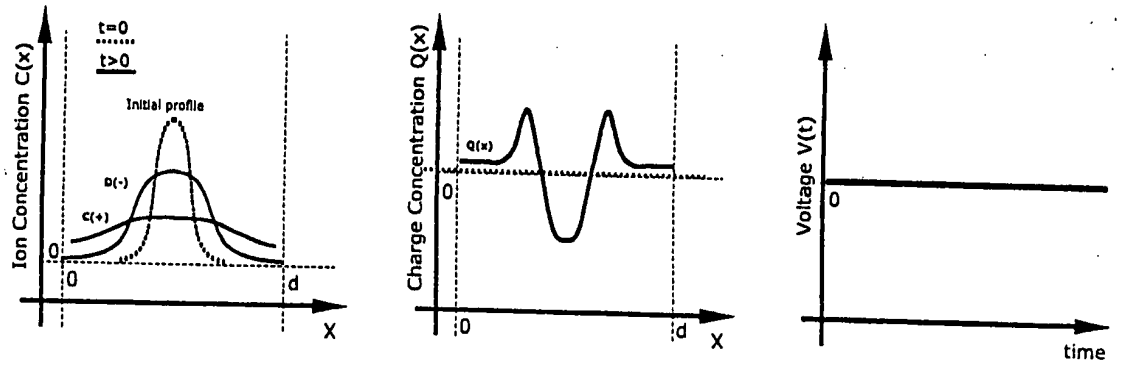
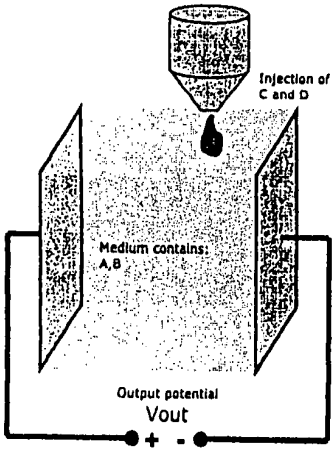
1.4 Potential difference between electrodes in none-equilibrium (transient) state:

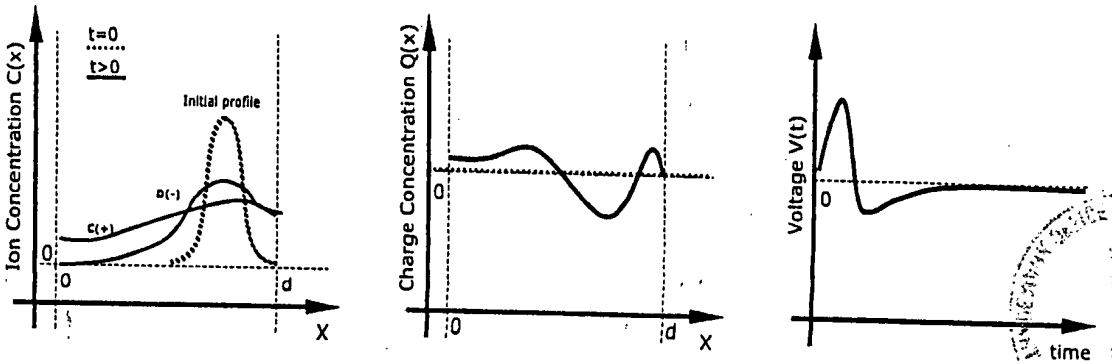
1) Electrodes are inert and do not interact with the medium.
2) Two molecules (ions) are present in the medium and two are added.
3) Molecules have arbitrary diffusion length and charge.
4) Background molecules are not shown (A and B).





1.4.a) C and D are added symmetric to the electrodes.

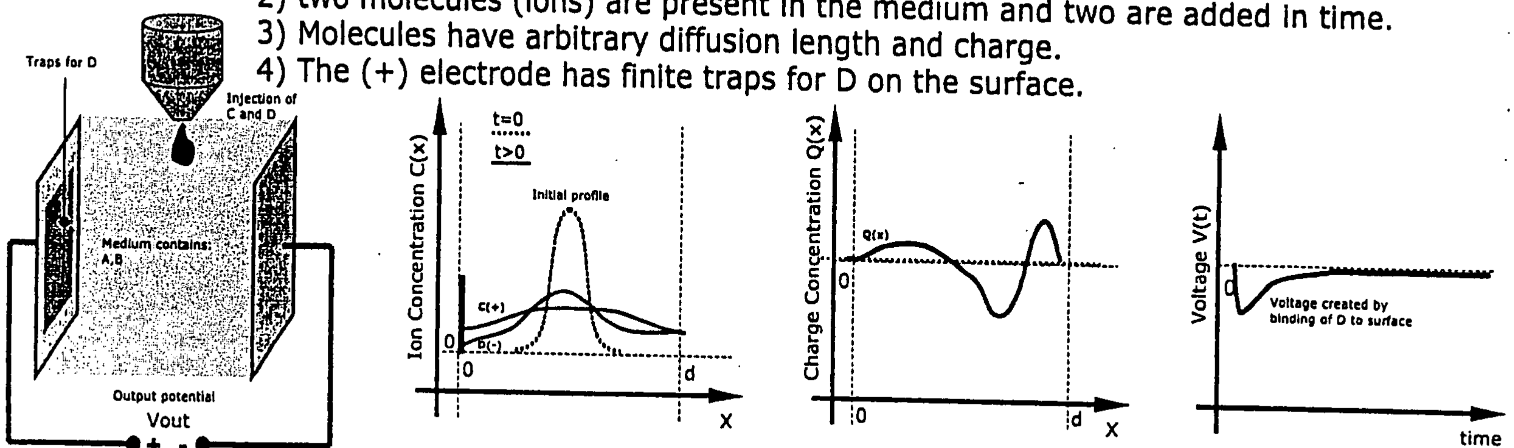




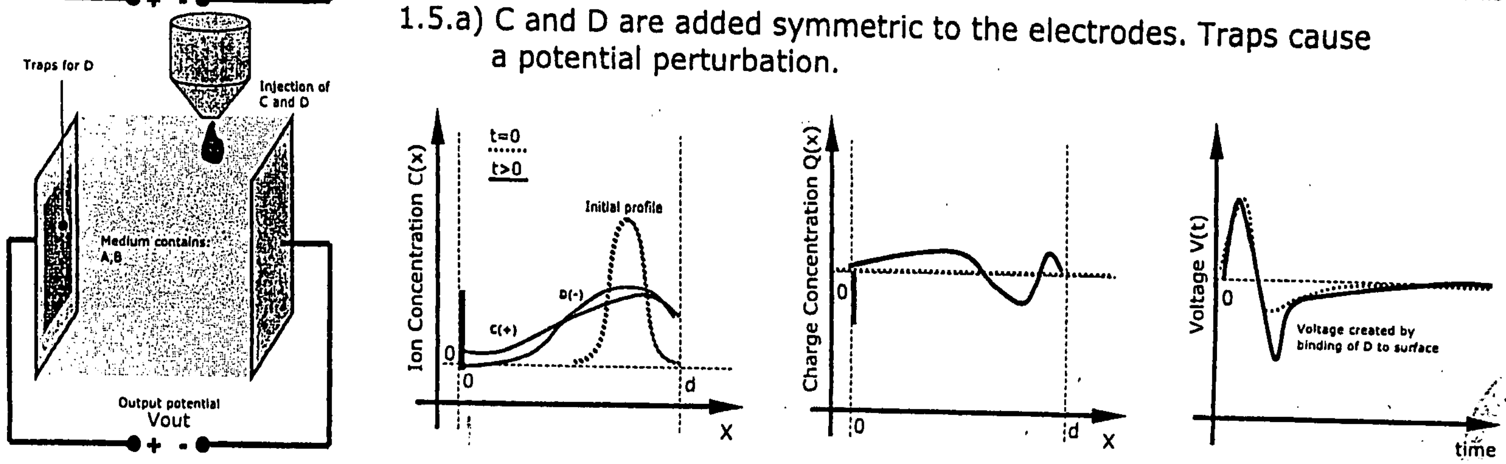
1.4.b) C and D are added asymmetric to the electrodes and an ionic perturbation is generated.

1.5 Potential difference between electrodes in the none-equilibrium (transient) with surface trap:

1) Electrodes are inert and do not interact with the medium.
2) two molecules (ions) are present in the medium and two are added in time.
3) Molecules have arbitrary diffusion length and charge.
4) The (+) electrode has finite traps for D on the surface.



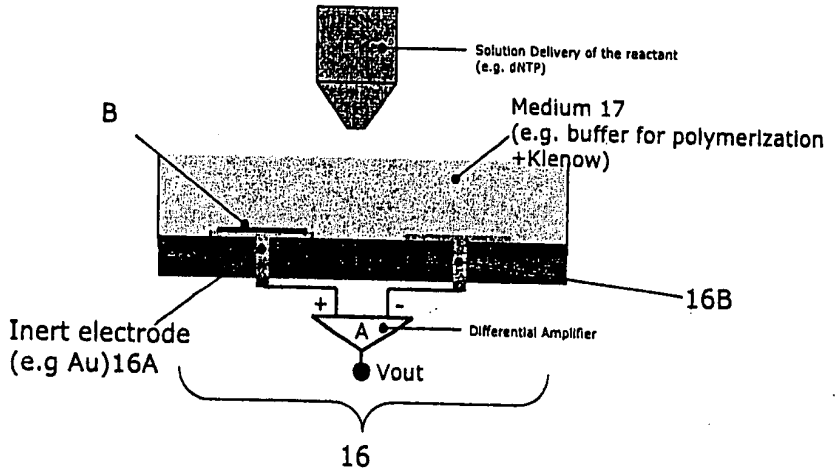
1.5.a) C and D are added symmetric to the electrodes. Traps cause a potential perturbation.



1.5.b) C and D are added asymmetric to the electrodes, and an extra electric field perturbation is created by the traps.

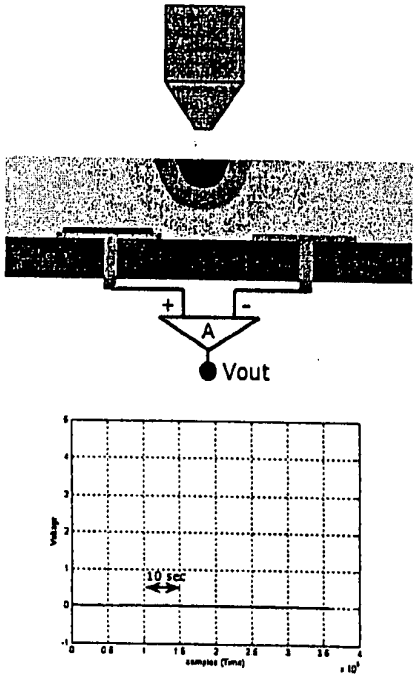
2.1 Planar sensor design example:

1) Electrodes are inert and do not interact with the medium.
2) The target molecules are immobilized on the (+) electrode.
3) The (-) electrode is the reference electrode.
4) A differential amplifier subtracts the voltage from the two electrodes.

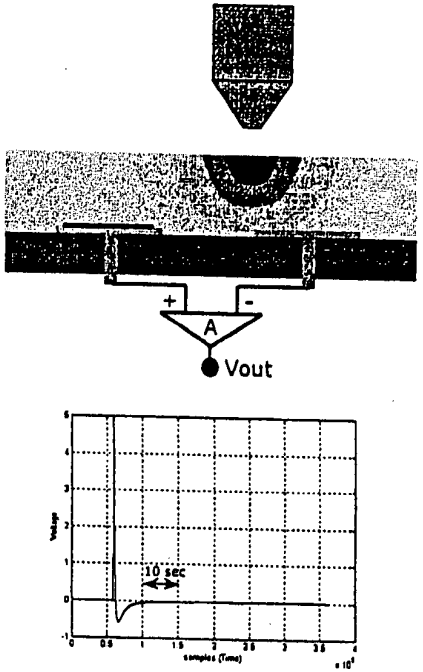


2.2 Example of signal generated when no binding at the surface occurs :

1) Electrodes are inert and do not interact with the medium.
2) The target molecules are immobilized on the (+) electrode.
3) The (-) electrode is the reference electrode.
4) A differential amplifier subtracts the voltage of the two electrodes.



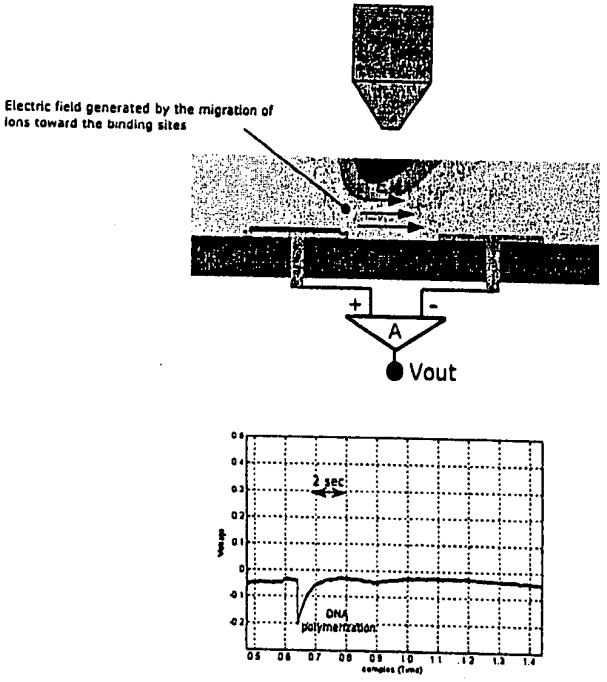
a) Solution is delivered symmetric to the electrodes
With 0.1 pmol immobilized ssDNA.



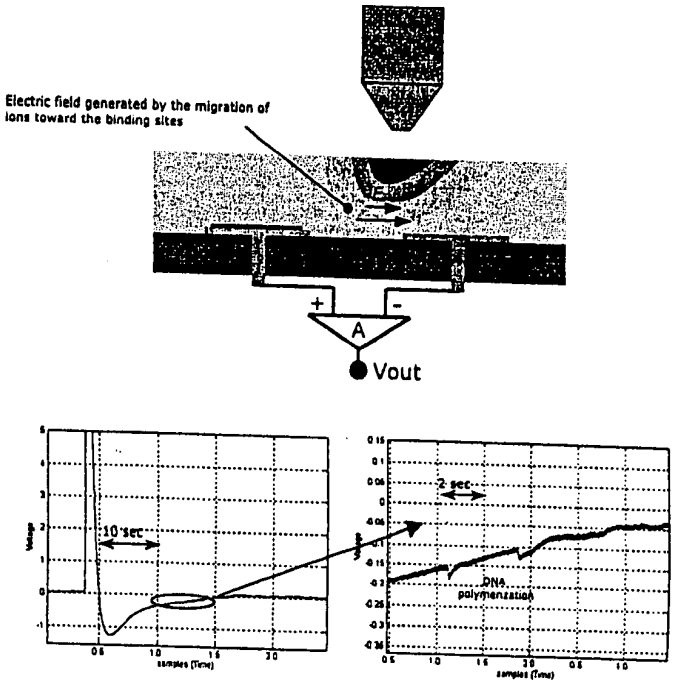
b) Solution is delivered asymmetric to the electrodes
With 0.1 pmol immobilized ssDNA.

2.3 Example of signal generated when <u>binding</u> at the surface occurs:

1) Electrodes are inert and do not interact with the medium.
2) The target molecules are immobilized on the (+) electrode.
3) The (-) electrode is the reference electrode.
4) A differential amplifier subtracts the voltage from the two electrodes.

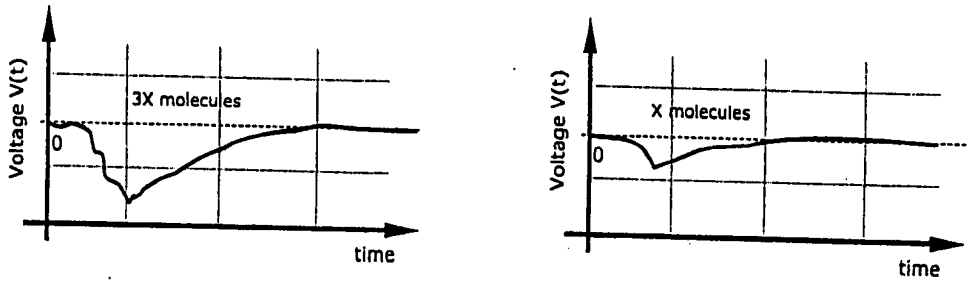


a) Solution is delivered symmetric to the electrodes, Polymerization of 0.1 pmol primed ssDNA.

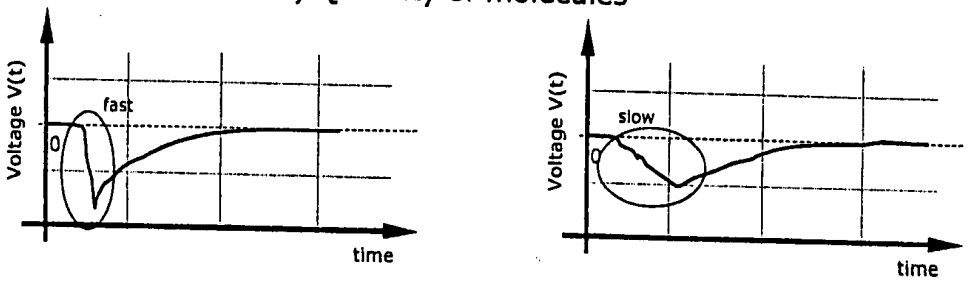


b) Solution is delivered asymmetric to the electrodes Polymerization of 0.1 pmol primed ssDNA.

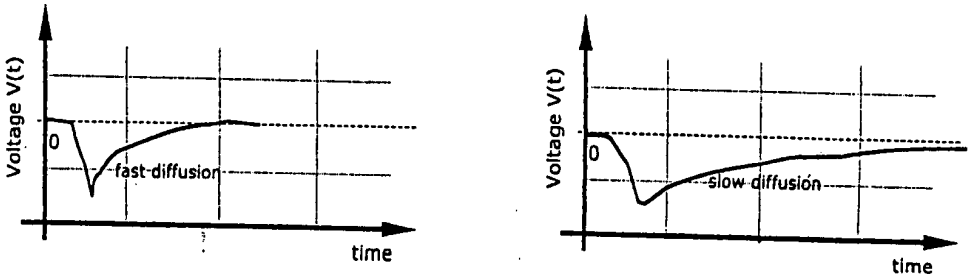
2.4 Analysis examples of the transient signal generated:



a) Quantity of molecules



b) Kinetics (speed) of the reaction



a) Movement and diffusion of molecules.

FIGURE 3:
Sequencing

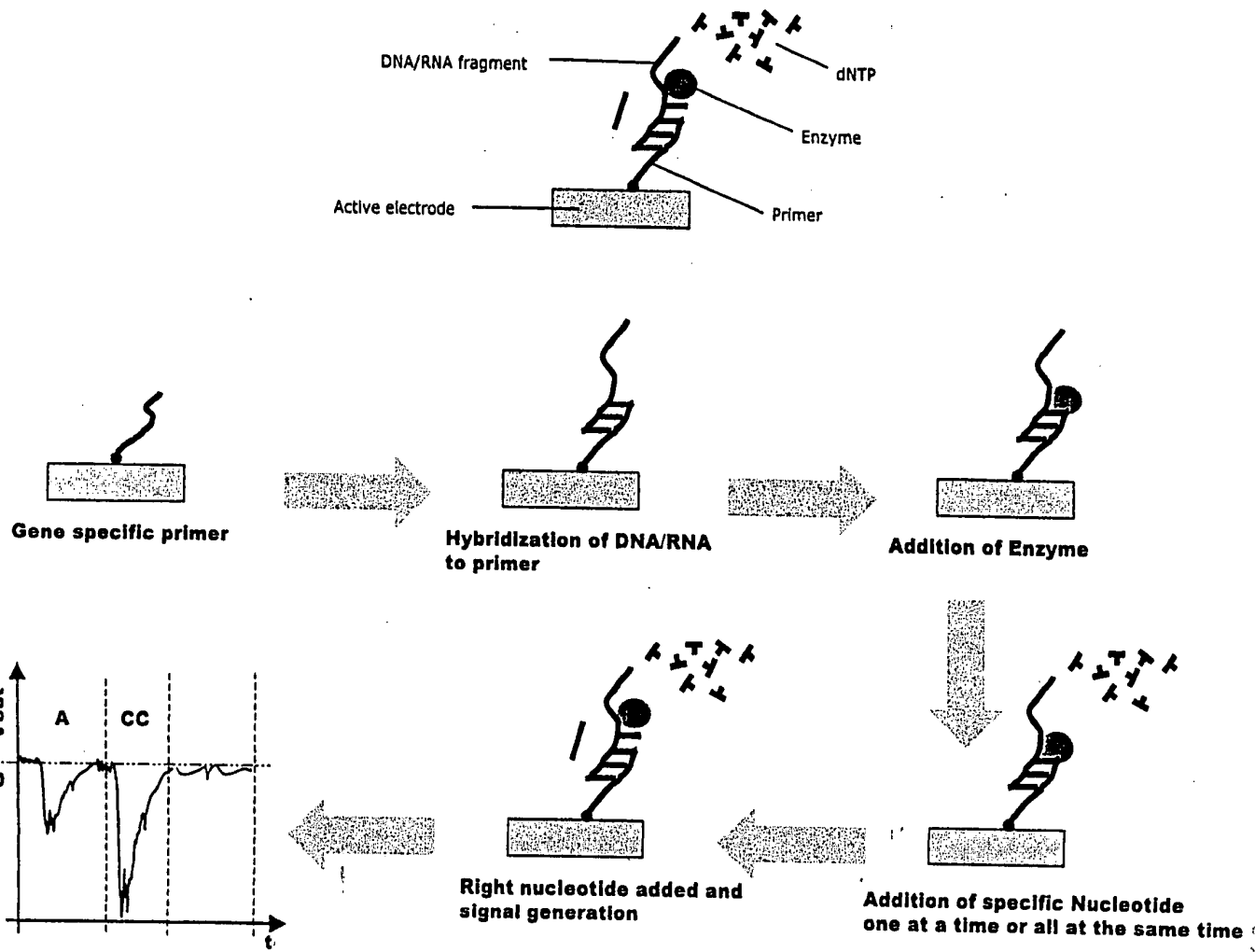


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FIGURE 4:1
SNP detection by using Total RNA

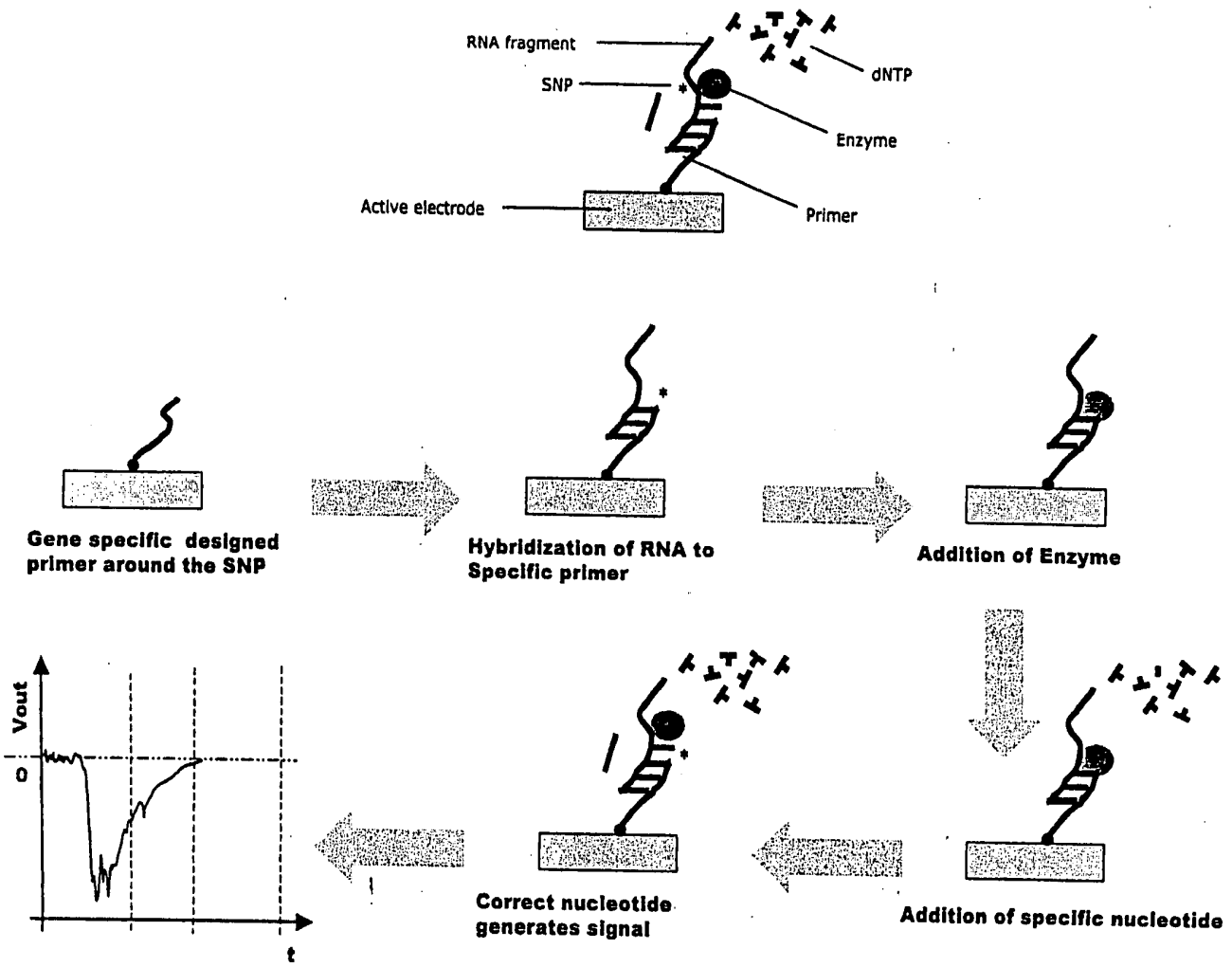

FIGURE 4:2
SNP detection by using cDNA

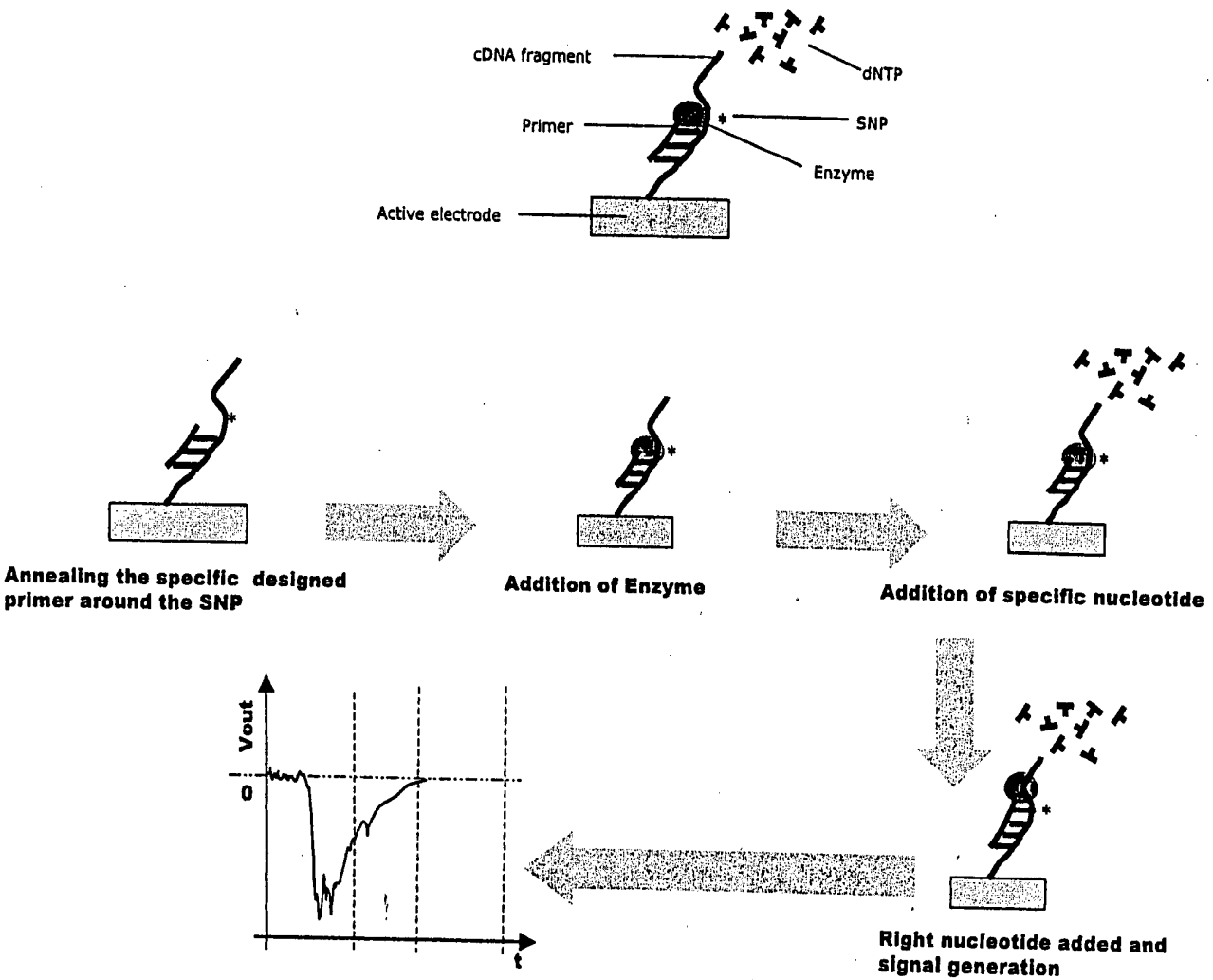

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FIGURE 4:3
SNP detection by using allele specific primer

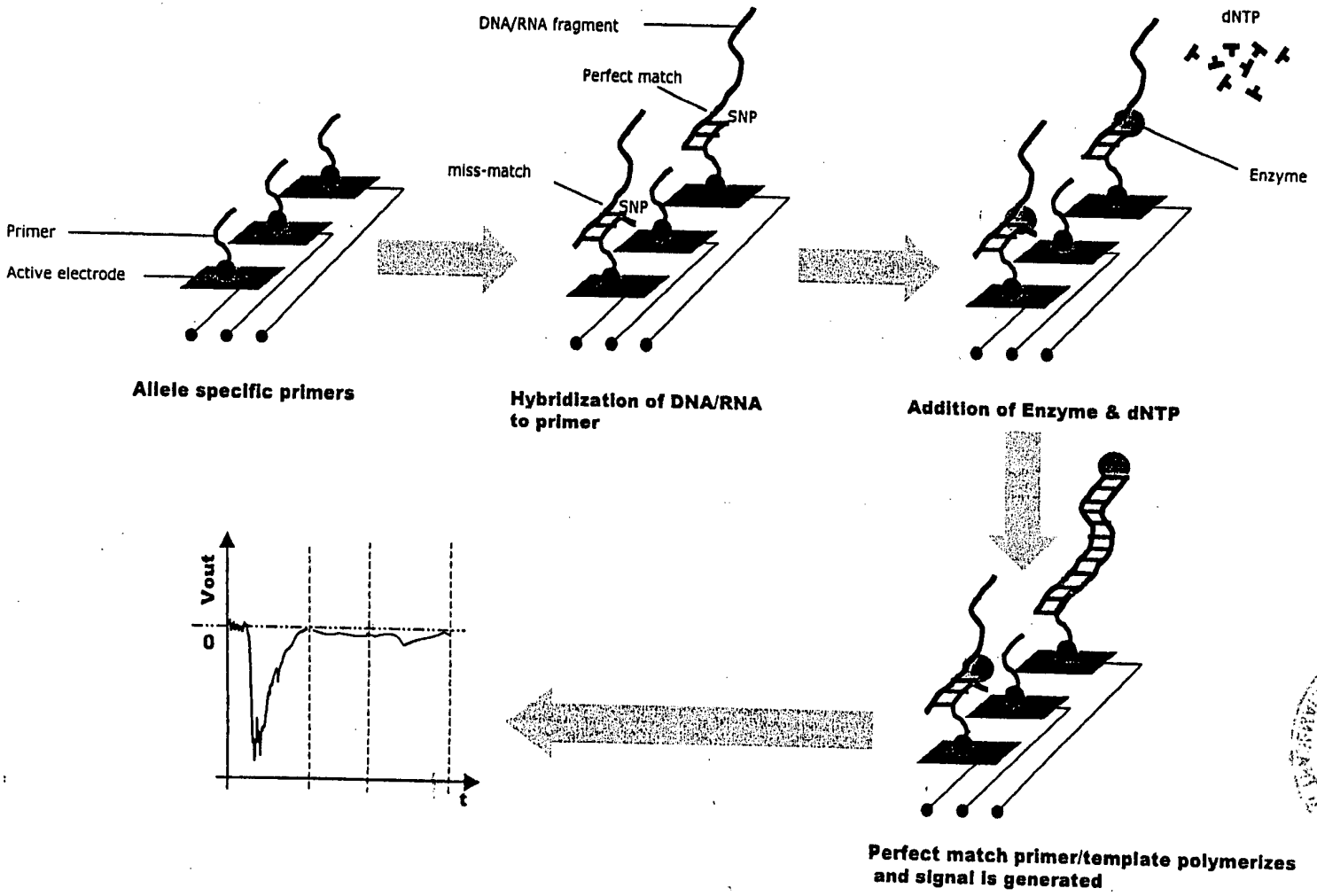

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FIGURE 5:
SNP detection by using PCR product

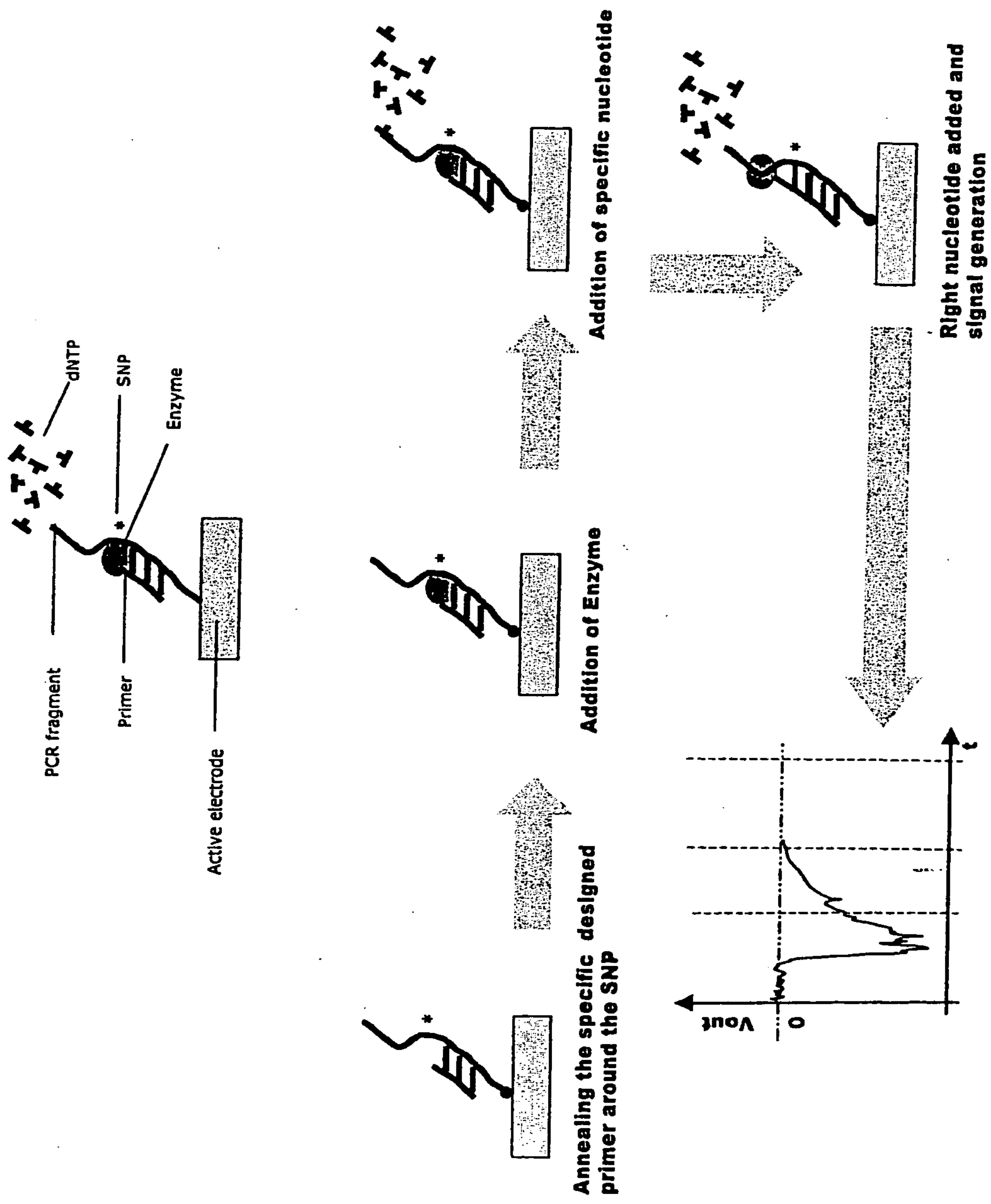

FIGURE 6:
SNP detection by using Exonuclease/ Degrading enzyme

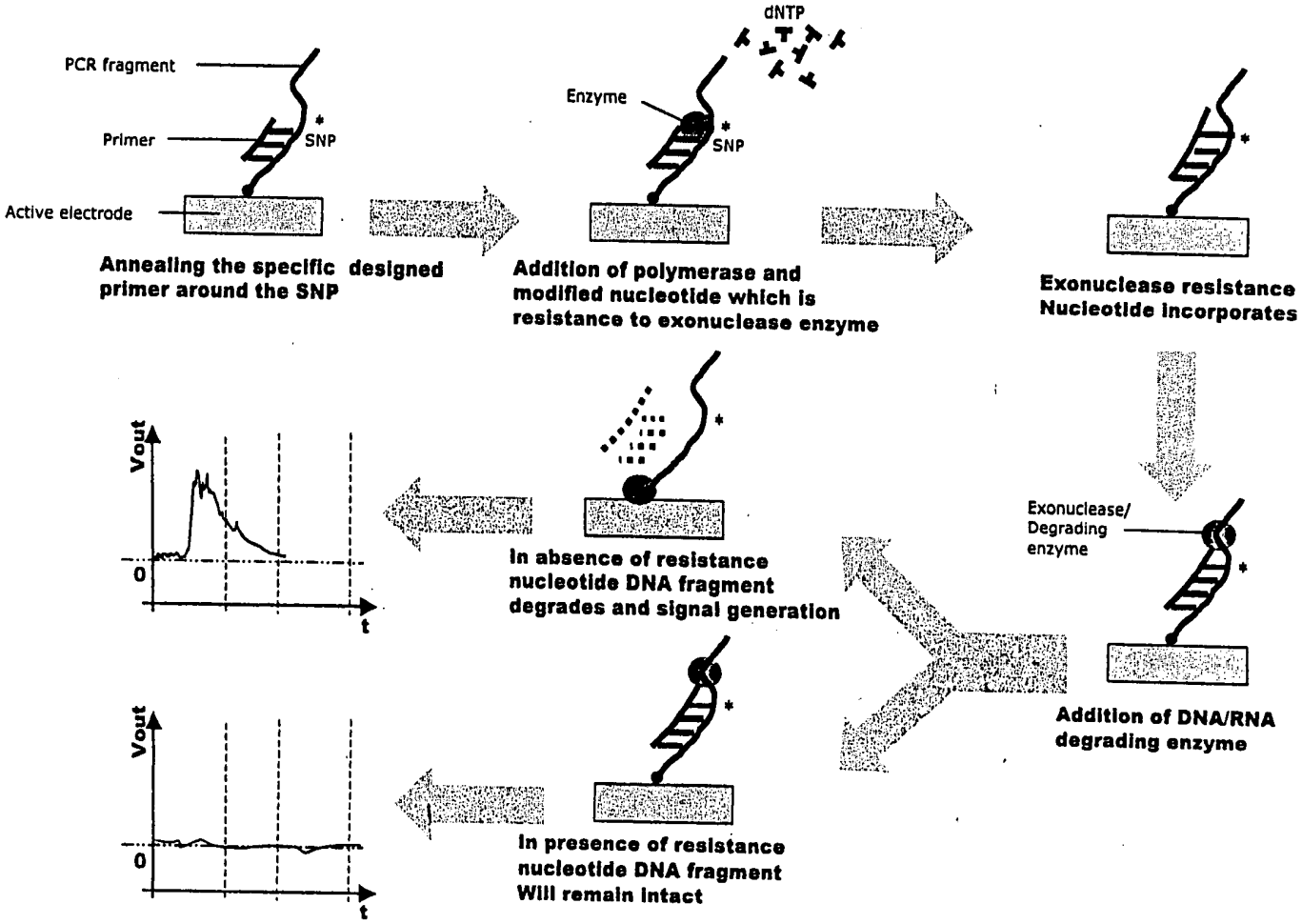

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FIGURE 7:
Real time PCR

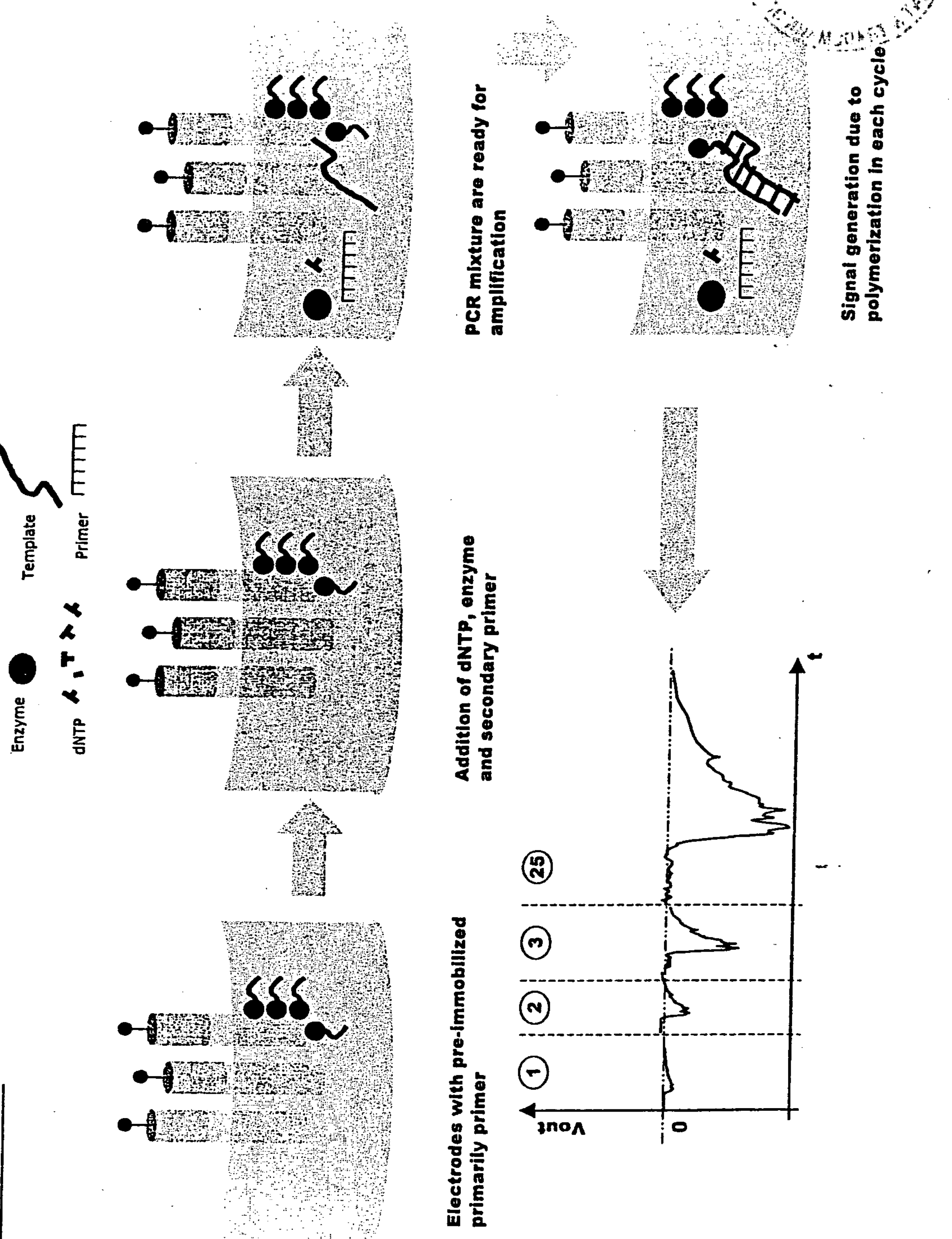

FIGURE 8:
Pathogen typing

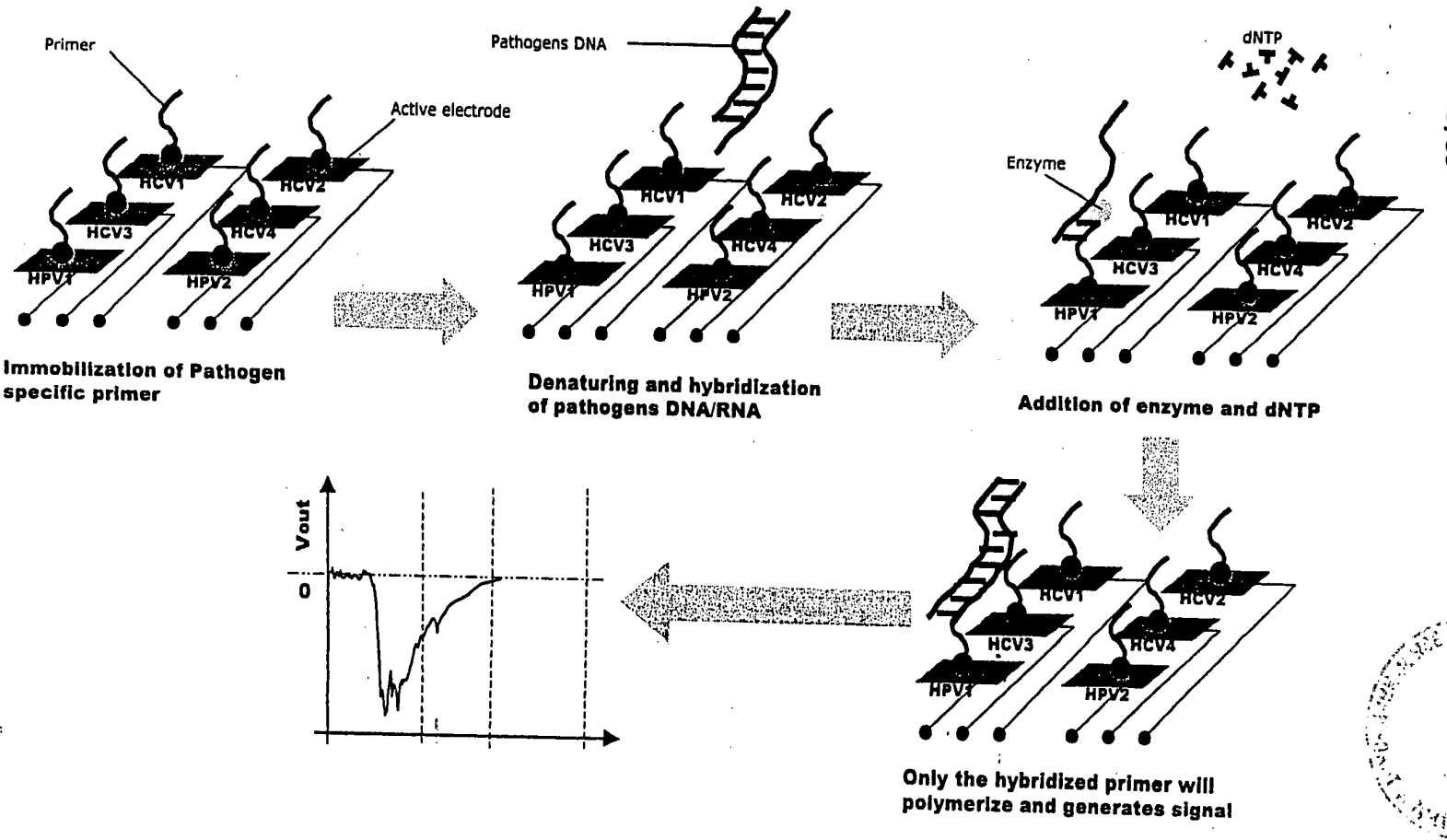

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FIGURE 9:
Antigen-antibody detection

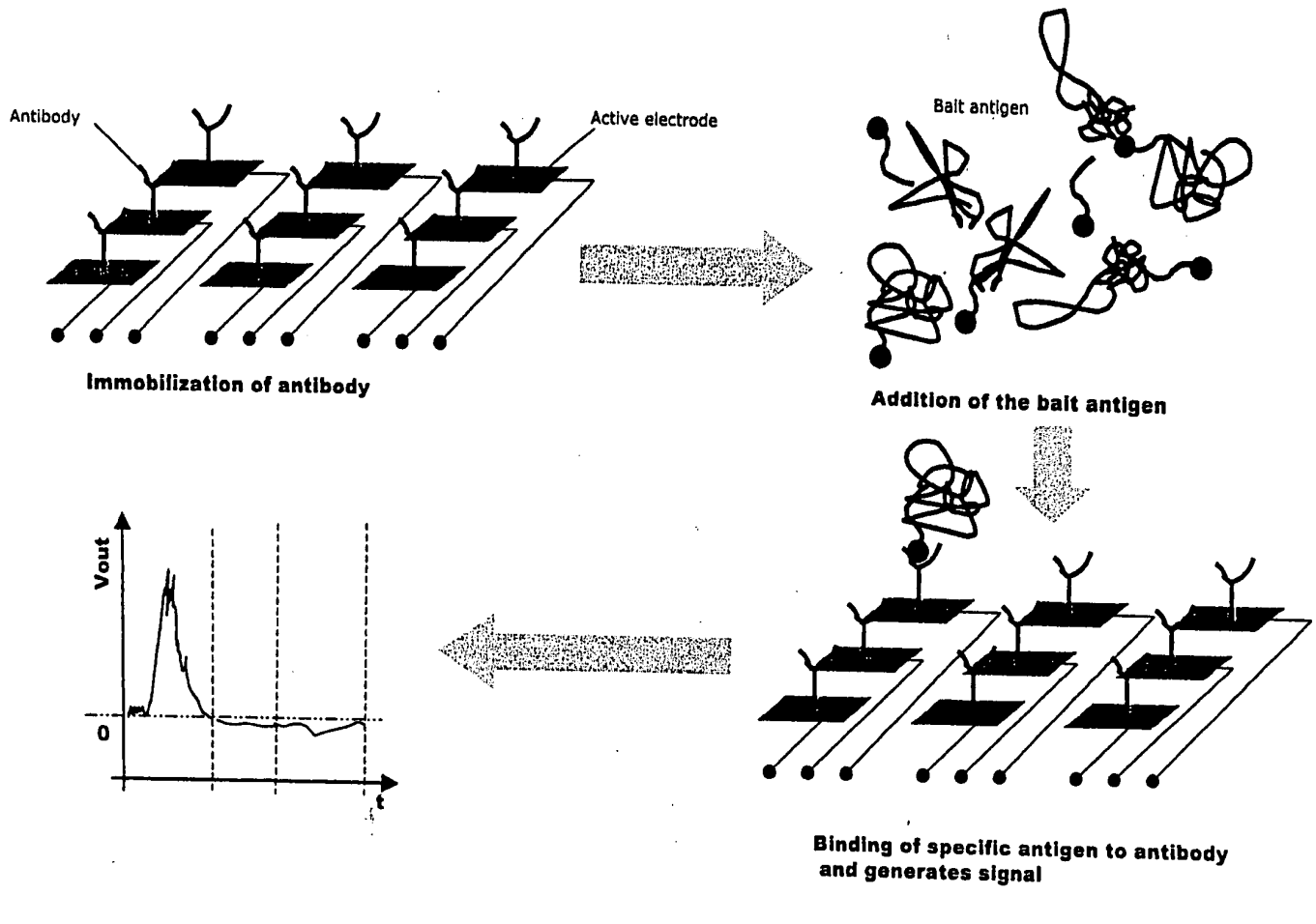

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FIGURE 10:
Protein-protein interaction

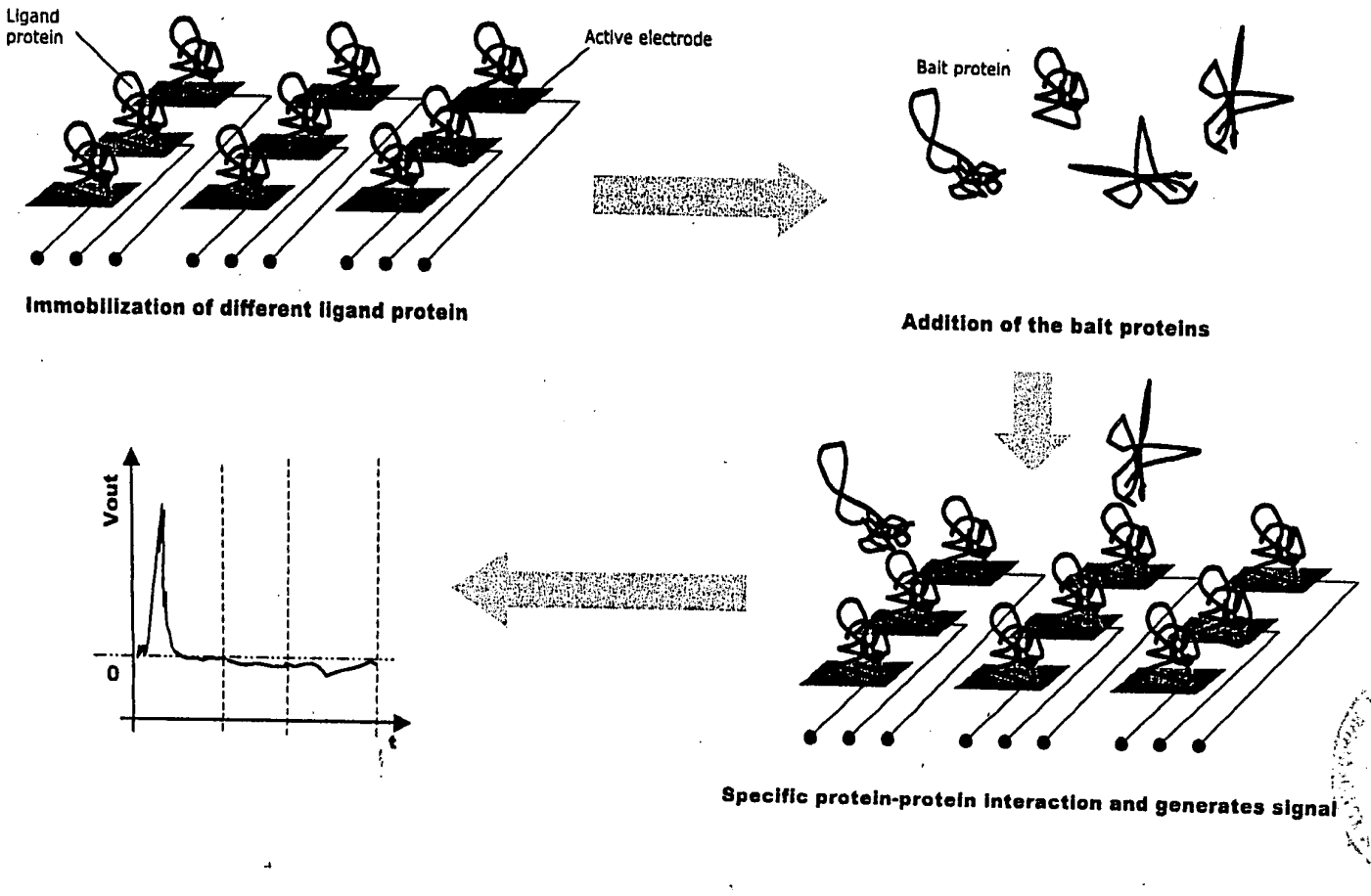


FIGURE 11:
Ligand and receptor detection

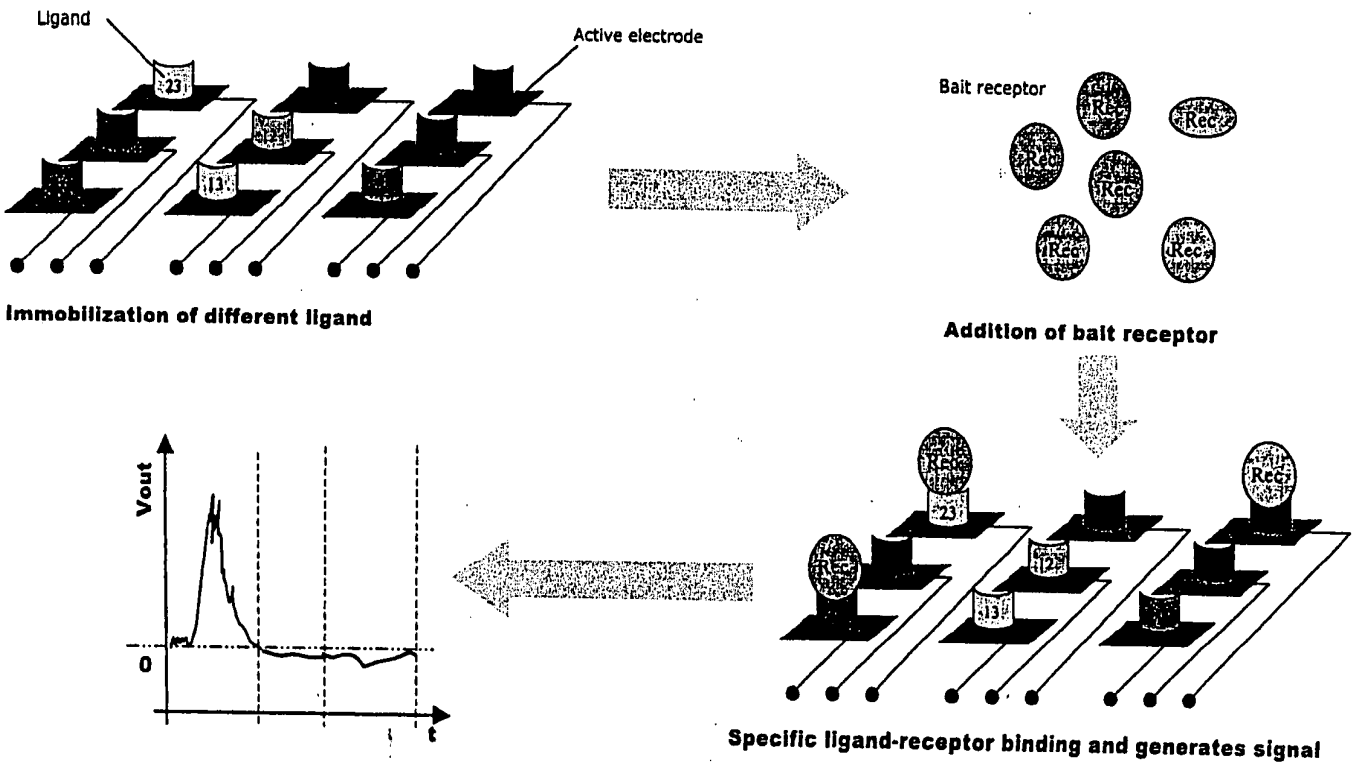
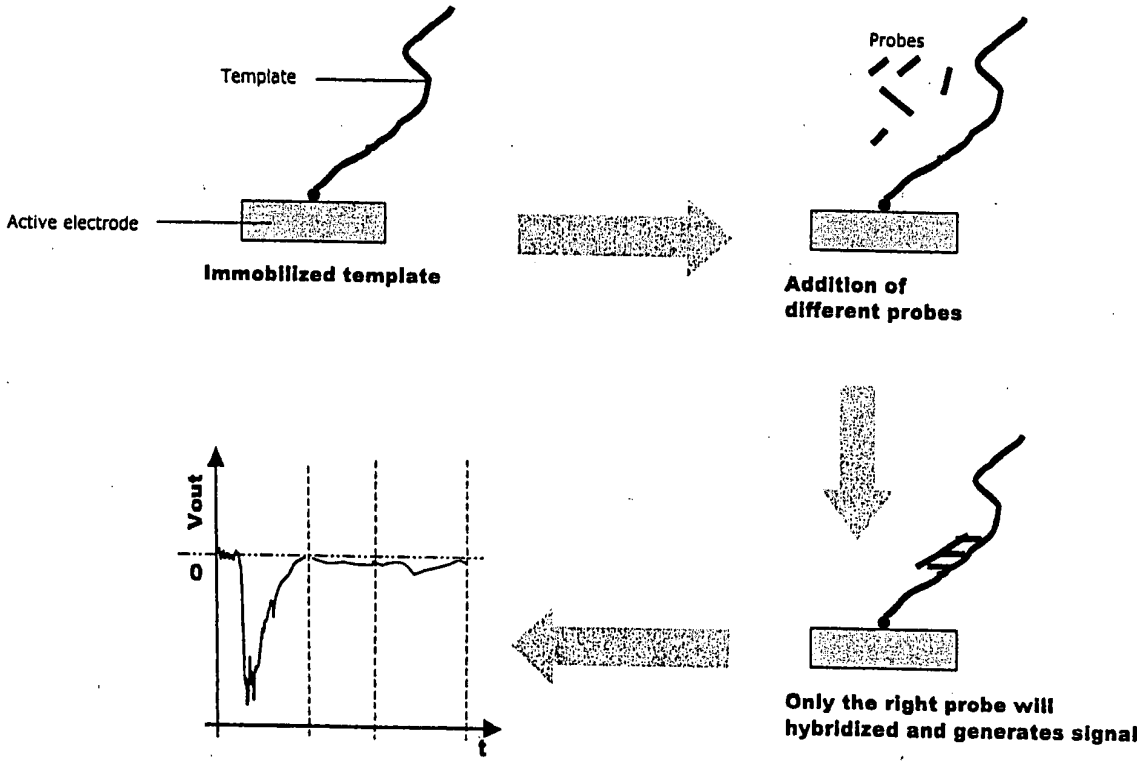


FIGURE 12:
Hybridization



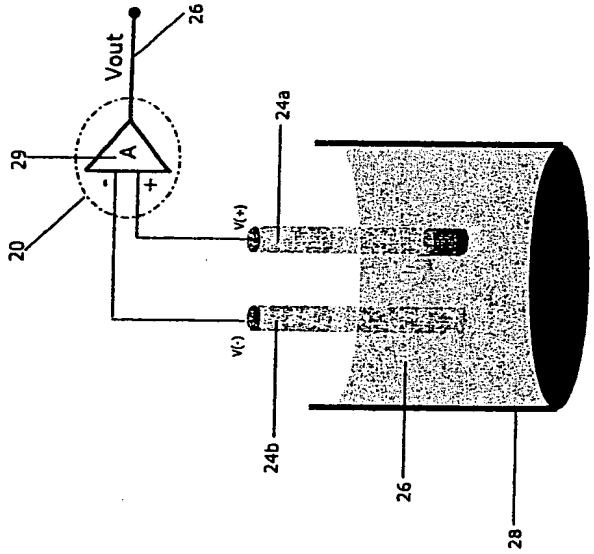


Fig: 13

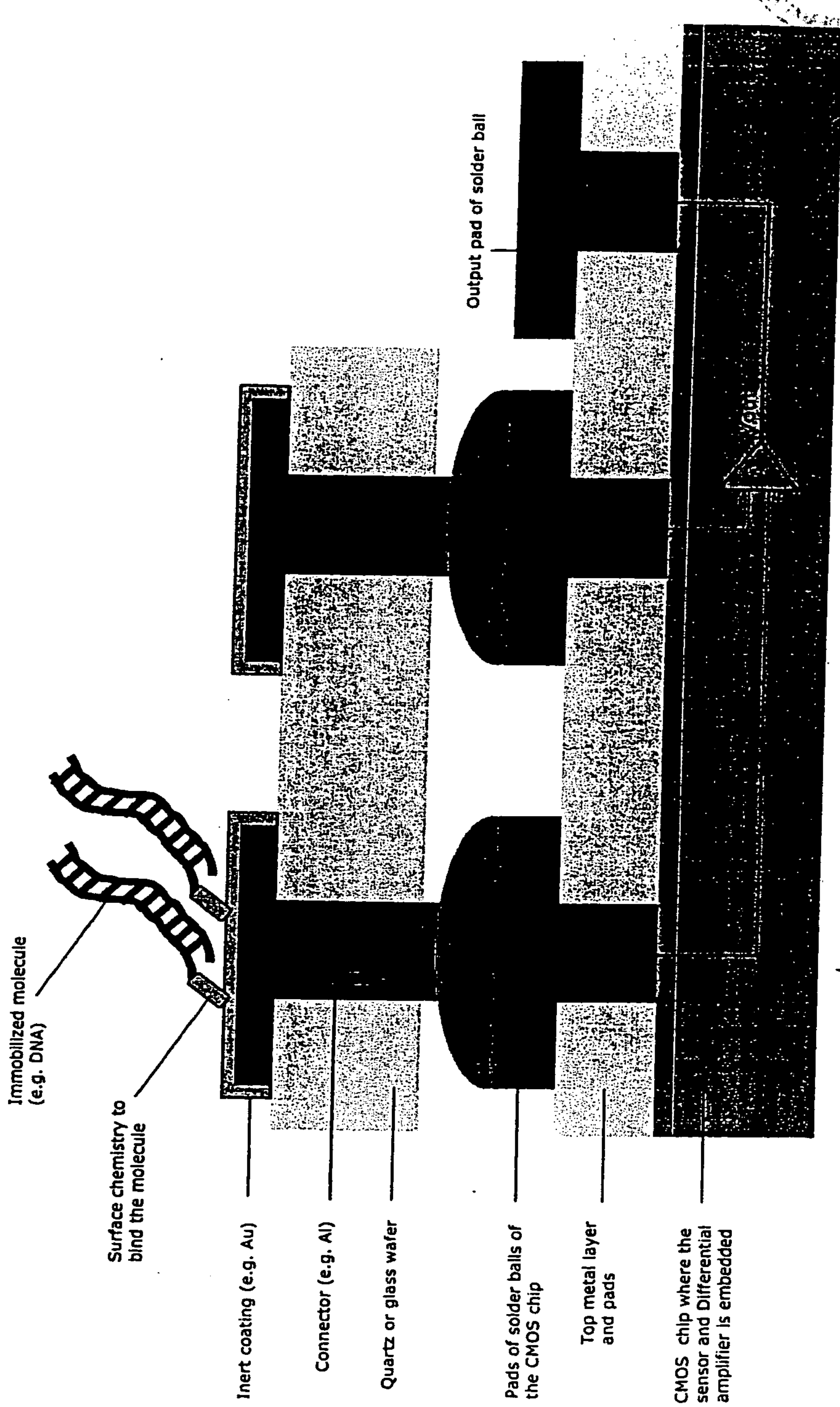


Fig: 14

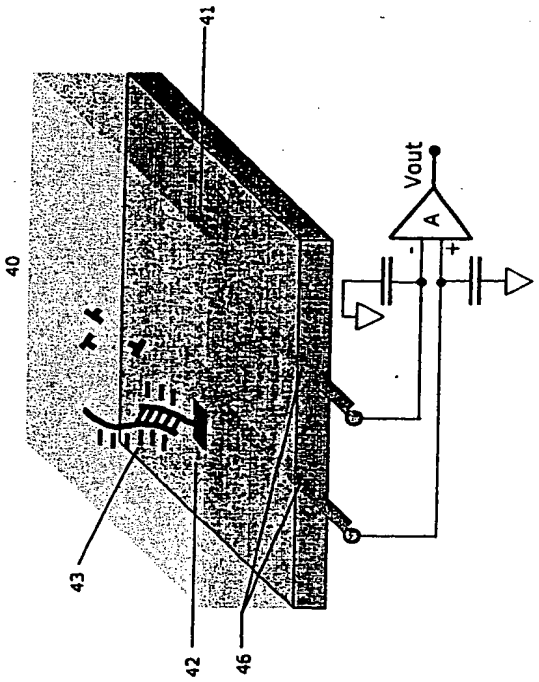


Fig: 15

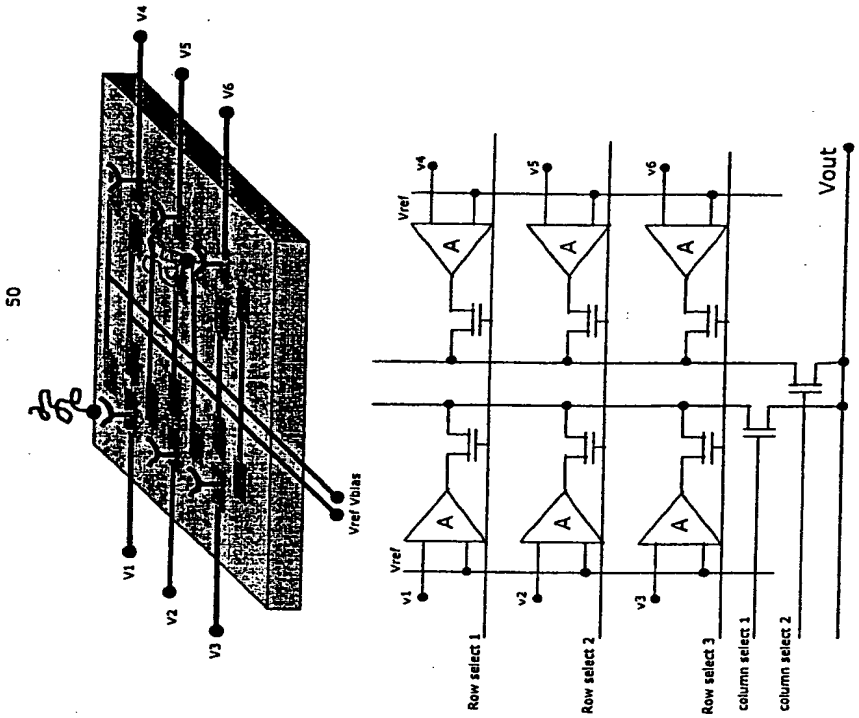


Fig: 16

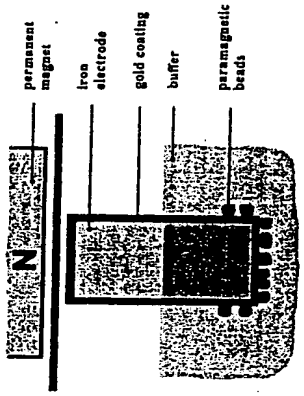


Figure 17A: PCR product attracts to an electrode by using a permanent magnet and paramagnetic beads.

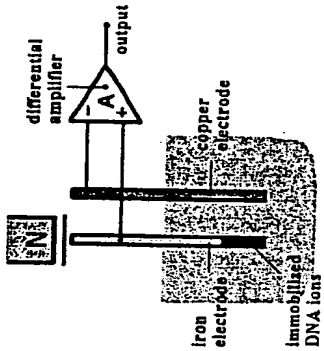


Figure 17 B: Basic model of the sensor with a differential amplifier

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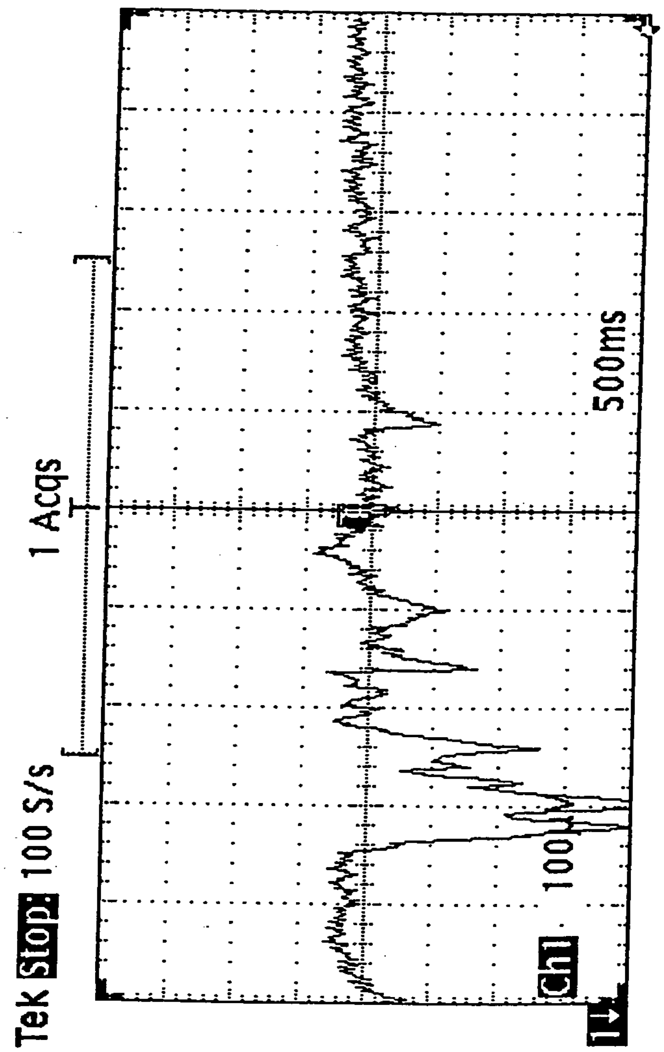


Figure 18 A: some sample charge sequencing extension signatures for 300 bp DNA

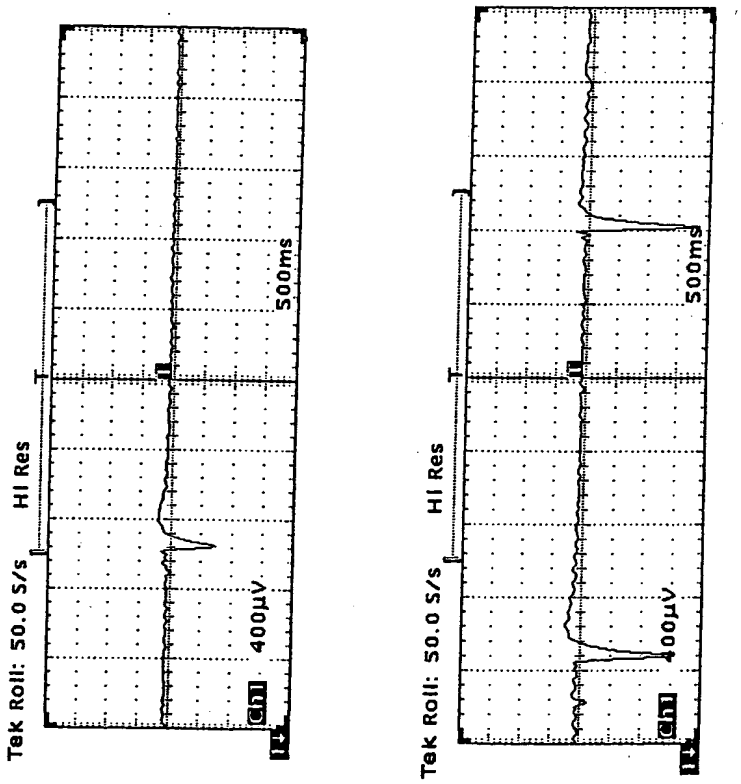


Figure 18 B: More sample charge sequencing extension signatures for 300 bp DNA with two different concentration of immobilized DNA (0.05 pmol and 0.1 pmol)

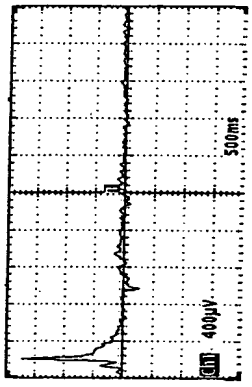


Figure 18C.

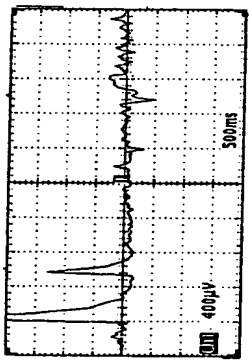


Figure 18D.

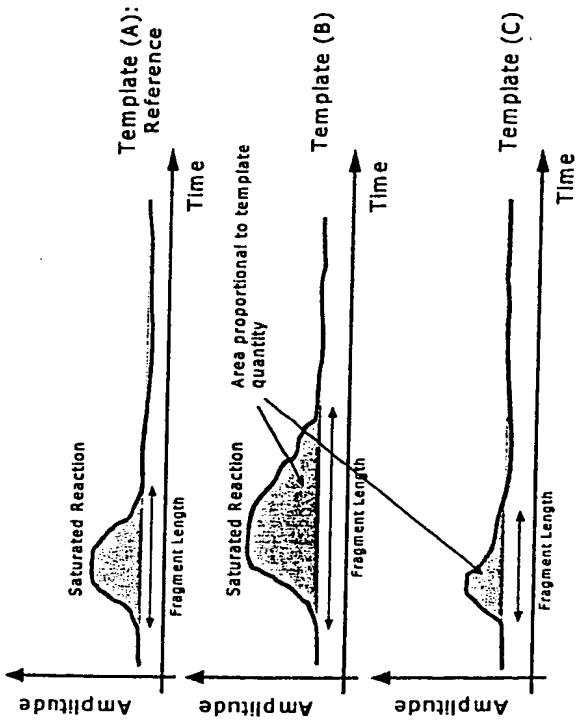


FIGURE 18E

FIGURE 19 a:
Gene Expression profiling by using Total RNA

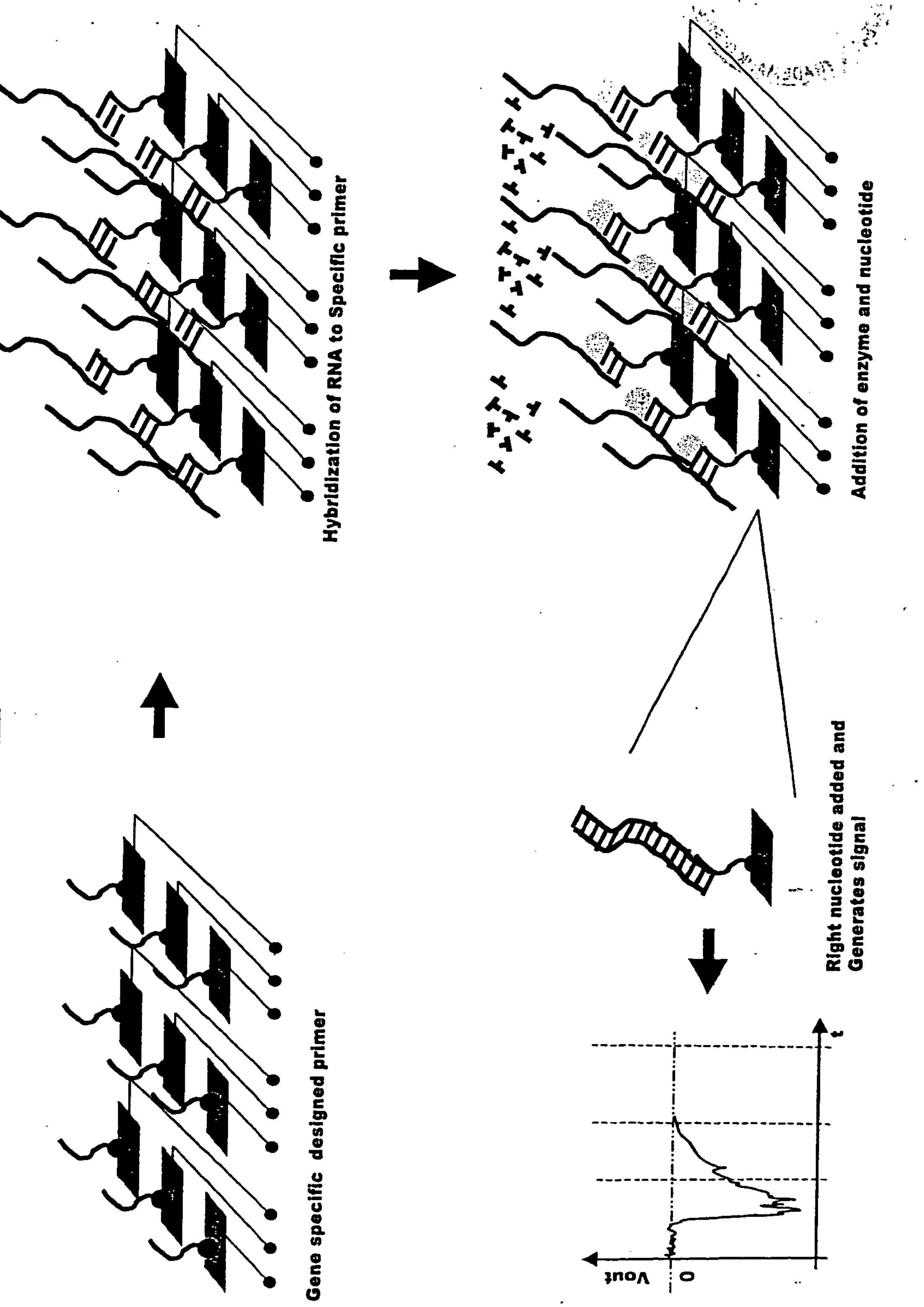
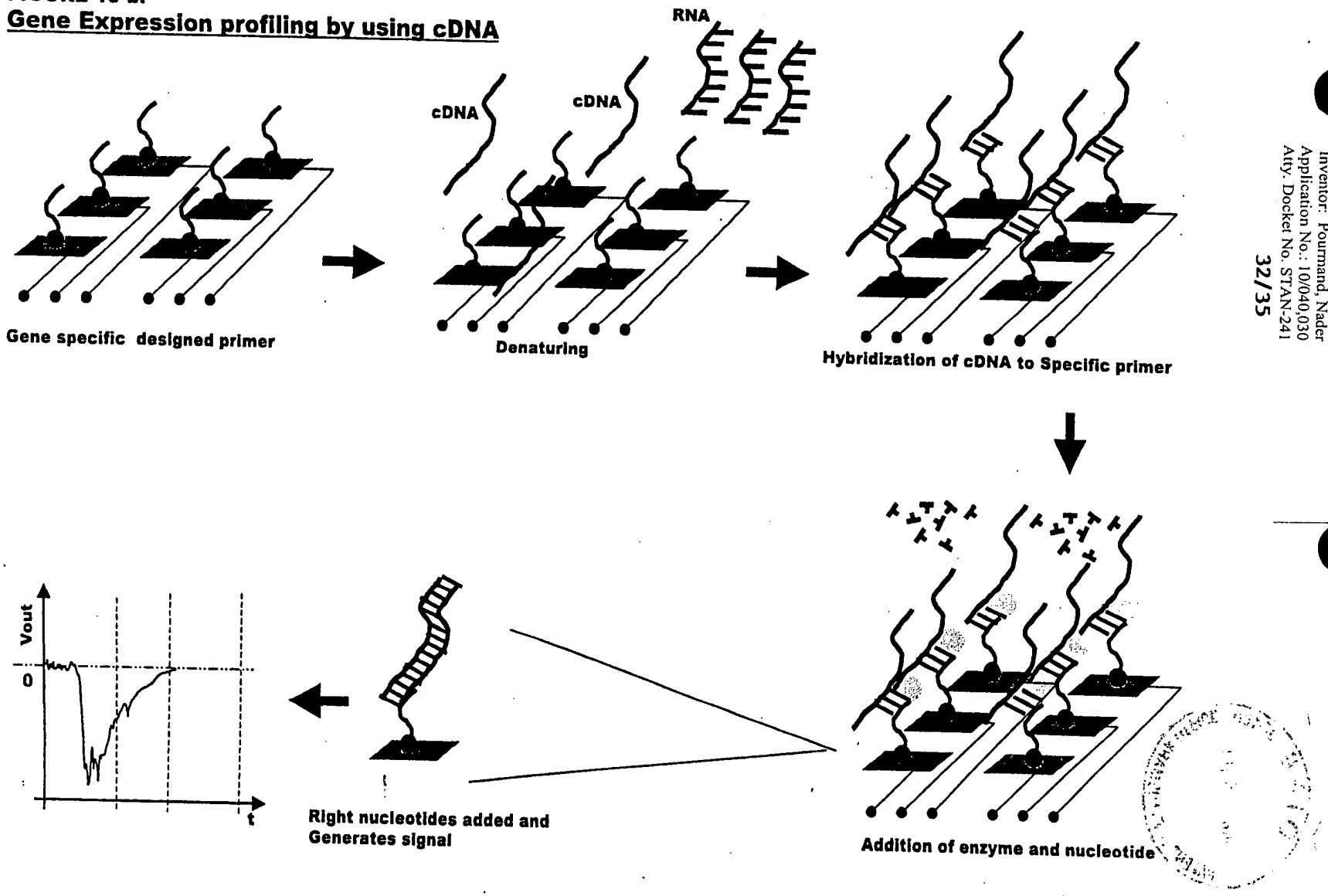


FIGURE 19 b:
Gene Expression profiling by using cDNA



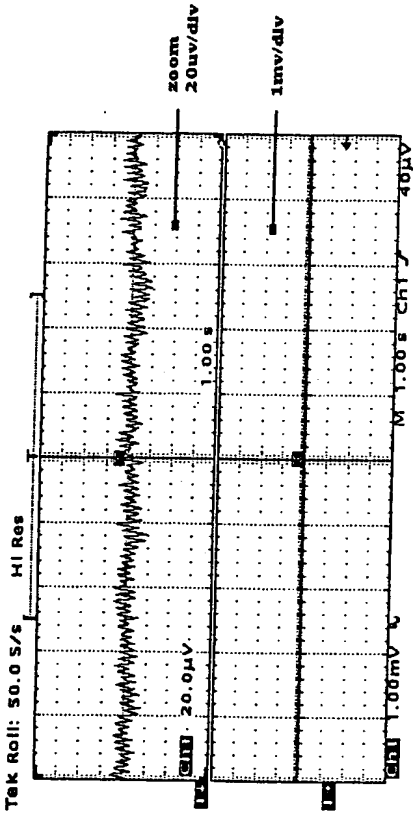


Figure 20

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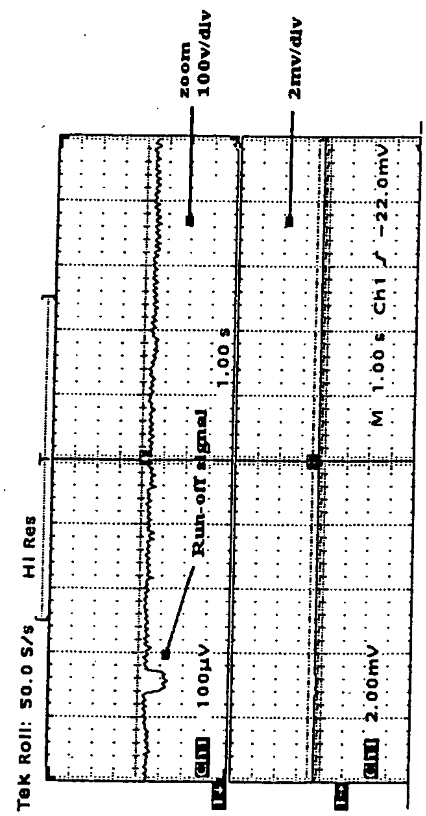

Figure 21

Figure 22